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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/531,435	10/07/2005	Patrick Joseph Silcock	AJPARK30.001APC	8251
20995	7590	04/02/2008	EXAMINER	
KNOBBE MARTENS OLSON & BEAR LLP			LIU, SAMUEL W	
2040 MAIN STREET			ART UNIT	PAPER NUMBER
FOURTEENTH FLOOR			1656	
IRVINE, CA 92614				

  

NOTIFICATION DATE	DELIVERY MODE
04/02/2008	ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

jcartee@kmob.com  
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<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/531,435	SILCOCK ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	SAMUEL W. LIU	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 12/20/07.  
 2a) This action is **FINAL**.                    2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 19-51 is/are pending in the application.  
 4a) Of the above claim(s) 44 is/are withdrawn from consideration.  
 5) Claim(s) \_\_\_\_\_ is/are allowed.  
 6) Claim(s) 19-43 and 45-51 is/are rejected.  
 7) Claim(s) \_\_\_\_\_ is/are objected to.  
 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on 15 April 2005 is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413)
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	Paper No(s)/Mail Date. _____ .
3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)	5) <input type="checkbox"/> Notice of Informal Patent Application
Paper No(s)/Mail Date <u>4/15/05</u> .	6) <input type="checkbox"/> Other: _____ .

## **DETAILED ACTION**

### *Status of the claims*

Claims 19-51 are pending.

The amendment filed 12/20/07 which cancels claims 1-18, amends claims 27-28, 31, 35, 37, 39 and 41-43 has been entered.

### *Continuation data and priority*

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119 (a)-(d). The certified copy has been filed in New Zealand Application. 522071 filed 10/18/02.

### *Election/Restrictions*

The Applicants' election (filed 10/7/07) of Group III, claims 19-43 and 45-51 without traverse is acknowledged. Claim 44 is withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Claims 19-43 and 45-51 are examined in this Office action.

### ***IDS***

The references cited in the IDS filed 4/15/05 have been considered by Examiner.

### *Objection to Spec*

The disclosure is objected to because of the following informalities:

- (1) At page 2, line 20, the meaning of "Ser(P)" is not apparent; does it refer to a phosphorylated serine residue or a photo-labeled serine?
- (2) At page 8, line "MAP" should be spelled out for the first instance of use.

(3) At page 12, last line, “Novo.45K” (see also page 3213), and “USP” need to be clarified. The Spec does not define it.

(4) At page 19, line 16, change “280  $\eta$ m” to “280 nm”.

(5) At page 32, line 18-21, the Spec sets forth 4 molecular weight ranges without “unit”.

### ***Objection to Claim***

In claim 50, “y the partial hydrolysis” should be changed to “by the partial hydrolysis” in view of the similar recitation of claim 51.

In claim 45, “comprises about 10 or more  $\mu$ mol” should be changed to “comprises about 10  $\mu$ mol or more”.

### ***Objection to drawings***

Figures 5-9 are objected to because “SMH” should be spelled out for consistency (see Figure 10).

Figures 13-14 are objected to because of lacking the “index” and “Unit” for the horizontal axis [e.g., phosphoprotein concentration (mM)].

### ***Claim Rejections - 35 USC § 112, second paragraph***

*The following is a quotation of the second paragraph of 35 U.S.C. 112:*

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 19-43 and 45-51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 19 recites “phosphoprotein preparation has been obtained by partially cross linking...”; the recitation is unclear whether or not said preparation actually comprises the cross linked phosphoprotein or/and non-cross linked phosphoprotein, because the phrase “...obtained by partially cross linking a partial hydrolysate of casein” cannot substitute for the “... are partially cross-linking a partial hydrolysate of casein”, and because the “partially cross linking” process results in non-cross linked product; and thus, the preparation “obtained” may not necessarily comprises the crossed linked product thereof. Similarly, see also claims 20 and 45. Claims 20-43 which depend from claims 19 and 20 are also rejection.

Claim 22 recites “total number of peptide bond”; the recitation is unclear as to which protein(s) the “peptide bonds” refer; does it refer to the “peptide bonds” of total polypeptide/peptides in said “preparation” (due to the opened claim language “comprises”), or solely refers to the “peptide bonds” of a phosphoprotein casein sequence, e.g., casein? In addition, claim 22 lacks antecedent basis for “the degree of hydrolysis” because in claim 19 form which claim 22 depends does not set forth the “degree” thereof. Similarly, see claims 23-24 and 28-30.

Claims 23-24 is indefinite because the claims do not make it clear what is the subject of “about 3.5% to about 7% (claim 23) and “about 4% to about 6.5% (claim 24).

Claims 25 and 26 recite the limitations “10% or less” and “5% or less”, respectively. The metes and bounds of the lower-limit (“or less”) of the limitations is unclear; does it include “0%”? Given that it is “0%”, it would render the claims indefinite.

Claim 28 recites “about 10 or more  $\mu$ mole cross links”; the up-limit (“or more”) of the recitation is unclear; does it include “100%”? Given that it is “100%” “ $\mu$ mole cross links”, then, it is contrary to the “partial cross linking” recited in claim 19 from which claim 28 depends; and thus, this would render the claims indefinite. Also, Claim 28 is unclear in “per gram of protein”; to what does the “protein” refer? Does the “protein” refer to (i) total phosphoprotein” in the preparation, or/and (ii) the cross-lined or uncross-linked phosphoprotein molecules; or (iii) any proteins contained in the preparation? Similarly, see also claims 29-30.

Claim 34 recitation “milk calcium” is awkward and vague because neither the Spec nor the relative art teaches/defines the “milk calcium”. It is of note that “milk calcium” is uncommon term in the art and has no difference from the isolate calcium in chemical structure and function.

Claim 35 recites “at least about 5 mmol calcium ions; the metes and bounds of the up-limit of this recitation is not apparent; does it include umlimited amount of the calcium ions? Similarly, see also claim 36.

Claim 37 recites the limitation “...in the range of about 0.8-1.2:0.4-0.8”; the recitation is vague because the metes and bound of “about 0.8-1.2:0.4-0.8” is ambiguous; it is not apparent whether or not “about” is applied to both “0.8” and “1.2” or individually to “0.8” or “1.2” only. Similarly, “0.4-0.8”needs clarification.

Claim 45 recites “about 10 or more μmole cross links of protein”; the recitation is unclear in the following three aspects.

(1) The claim only set forth the mean of how to “obtain” the disclosed “phosphoprotein preparation”; the claim *per se* does not recite the “phosphoprotein preparation” actually comprise the cross-linked casein polypeptides. Note that “obtained by partially cross linking...” encompasses possibility of that the claimed phosphoprotein contains no cross link thereof.

(2) The up-limit (“or more”) is unclear; is it an unlimited amount of protein? Given that it is “unlimited”, then, it is contrary to the “partial cross linking” recited in the claim.

(3) Claim 45 is unclear in “...per gram of protein”; to what does the “protein” refer? does said “protein” refer to (i) total casein proteins in the preparation, or/and (ii) the cross-lined or uncross-linked casein proteins. (iii) does “total number of peptide bonds” count for sum of the “peptide bonds” of any proteins including “casein” in the claimed “phosphoprotein preparation”? The dependent claims are also rejected.

Claims 46-47 is indefinite because of lack of the subject of “about 3.5% to about 7% (claim 46) and “about 4% to about 6.5% (claim 47).

Claim 48 is unclear in “per gram of protein”; does the “protein” refer to any protein or total proteins in the claimed “phosphoprotein preparation? Similarly, see claim 49.

Claims 50 and 51 recite “...about 10% or less...”, and “...about 5% or less...”; the recitation is unclear as to what is the lower-limit (“or less”) of the “degree of hydrolysis”. Does “or less” encompass zero?

***Claim Rejections - 35 USC §102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

• Claims 19-27, 31-34, 37-38, and 45-48 are rejected under 35 U.S.C. 102(b) as being anticipated by Lauber et al. (*Nahrung/Food* (2001, June) 45, 215-217).

Lauber et al. teach UHT milk, a nutritional composition, comprising “casein oligomerization” (page 216, left column), i.e., cross-linked casein which is equivalent to instant partially cross linked casein. Since the limitation “obtained by ...” in claims 19 and 45 is considered to be a mean of producing the cross linked casein, and since the same end-product can be made from different production means and the means will not alter chemical property of end product,

i.e., “cross linked casein”, Lauber et al. teach the composition of claim 19.

Lauber et al. teach the cross-linked caseins are about 2.04 mmol per 100 g protein (page 216, right column, first paragraph, line 7-8 and Table 1), i.e., ~ 0.02 mmol/g, or ~ 20  $\mu$ mol/g protein, which anticipates claims 45, 48 and 29.

Because UHT milk contains endogenous proteases including trypsin which hydrolyze the milk proteins such as caseins [see “*Discussion of art*” [6]], the UHT inherently comprises the casein hydrolysate resulted from the protease hydrolysis thereof. Therefore, Lauber et al. inherently teach claims 20-21.

Claims 22-24 and 46-47 are directed to “%” of the hydrolysis of the casein. Since Table 1 shows incubation of UHT milk at 37 °C for different period of times (from 3 to 31 days), wherein the “hydrolysis” takes places prior to or during the casein oligomerization, i.e., cross linking. Because the hydrolysis is an inherent property of the HUT milk composition under the above discussed conditions, the limitations as to % of “partial hydrolysis” in claims 22-24 and 46-47 and 50-51 are therefore inherently taught by the above Lauber et al. teachings. Therefore, claims 22-24 and 46-47 are anticipated.

Similarly, claims 25-26 limitation “... rendered insoluble at pH7 by the partial hydrolysis” is considered to be part of the inherency discussed above,; and thus, claims 25 and 26 are also included in the rejection.

Lauber et al. teach that casein can be cross-linked by transglutaminase which catalyzes and increases casein oligomerization (see page 21, left column, lines 1-8, and page 217, left column, last two lines), which anticipates claim 27.

Since milk inherently contains calcium and calcium phosphate ions (see “*Discussion of art*” [7]), the above Lauber et al. teachings anticipated claims 31-34.

Because the calcium phosphate “ $\text{Ca}_3(\text{PO}_4)_2$ ” (see “*Discussion of art*” [2]) has ratio of  $\text{Ca}^{2+}$  to  $\text{PO}_4$  1: 0.6, the above Lauber et al. teachings inherently anticipate claims 37-38.

- Claims 19-26, 31-34, and 37-43 are rejected under 35 U.S.C. 102(b) as being anticipated by Reynolds E. C. (US Pat. No. 5981475).

In patent claims 1-13, Reynolds teaches a dentinal composition comprising a casein (claim 1) prepared by hydrolysis (col. 2, lines 33-39), and thus the product of said

hydrolysis is equivalent to instant "hydrolysate" (instant claim 20). Since the composition of instant claim 19, as written, does not necessarily comprise the cross-linked casein (see above corresponding discussion), Reynolds teaches claims 19-20.

\*It is noted that "for remineralizing ...." recited in claim 19 is considered to be intended use which ahs little patentable weight.

The above mentioned "hydrolysis" is performed by trypsin protease digestion (col. 3, lines 33-37), which anticipates claim 21.

Since insolubility of casein in neutral (pH 7) solution is inherent property of casein (see "*Discussion of art*" [2]), and since the limitation "hydrolysis is such that about 10% or less" in claim 25 broadly encompasses "0%" hydrolysis, claims 25-26 are included in the rejection.

The limitation of claims 22-24 is directed to the degree of the hydrolysis which is considered to be inherent by the above discussed "trypsin protease digestion"; and thus, claims 22-24 are included in the rejection.

Patent claim 7 discloses the composition comprising calcium ions, or calcium phosphate or phosphate ions, which anticipates claims 31-33.

Since the chemical property of "milk calcium" must be the same as that of ordinary calcium, claim 34 is anticipated.

In Example 2, col. 6, lines 55-57, Reynolds teaches that the composition also comprises strontium chloride, which anticipates claim 39.

In patent claim 10, Reynolds teaches that the composition further contains fluoride, which anticipates claim 40.

In Example 2, Reynolds teaches the composition is a toothpaste formulation, which anticipates claim 41.

Toothpaste is considered to be a colloidal dispersion or an emulsion (see “*Discussion of art*” [8]). Example 2 shows that “CPP” phosphoprotein is 5%. Thus, Reynolds’ toothpaste composition is in an emulsion form comprising 5% “CPP”. This inherently anticipates claim 42.

In the Table of Example 2, Reynolds teaches that the dentinal composition is formulated with “flavor” and “Xanthan gum” which are confection compounds. This anticipates claim 43.

Because the calcium phosphate “ $\text{Ca}_3(\text{PO}_4)_2$ ” (see “*Discussion of art*” [2]) has ratio of  $\text{Ca}^{2+}$  to  $\text{PO}_4$  1: 0.6, which inherently anticipates claims 37-38.

- Claims 19-26, 31-34, and 43 are rejected under 35 U.S.C. 102(b) as being anticipated by Reynolds et al. (US Pat. No. 5130123).

Reynolds et al. teach a dentifrice composition comprising a digest of a whole caseinate (see abstract and patent claim 1). Since the composition of claim 19 as written does not necessarily comprise the cross-linked casein or caseinate (see the above discussion of “...obtained by partially cross linking a partial hydrolysate of casein”, and see the rejection under 35 USC 112, 2<sup>nd</sup> paragraph), Reynolds et al. thus teach claim 19.

\* It is noted that “for remineralizing ....” recited in claim 19 is considered to be intended use which has little patentable weight.

The “digest of a whole caseinate” is equivalent to instant “partial hydrolysate” of casein. Thus, the Reynolds et al. teaching anticipates claim 20.

In patent claim 12, Reynolds et al. teach that the digest is a trypsin digest, which anticipates claim 21.

Since the “digest of a whole caseinate” taught by Reynolds et al. would inherently include the degree of “partial hydrolysis” set forth in claims 22-24. Thus, the above Reynolds et al. teachings also anticipate claims 22-24.

Since insolubility of casein in neutral (pH 7) solution is an inherent property of casein (see "*Discussion of art*" [2]), and since “hydrolysis is such that about 10% or less” in claim 25 encompasses no hydrolysis (“0%”), claim 25 is included in the rejection.

For the same reason, claim 26 is rejected.

In Examples 1 and 5, Reynolds et al. teach calcium alpha-s-casein, i.e., casein bound calcium ions, which anticipates claim 31.

In Example 4, Reynolds et al. teach the dentifrice composition, toothpaste further comprises mono sodium fluorophosphates, which is a source of phosphate ions; this teaches claim 32.

In Example 1, Reynolds et al. teach that the composition comprises "dibasic calcium phosphate", which anticipates claim 33.

Since "milk calcium" and ordinary/isolated calcium must have the same chemical property, claim 34 is rejected.

In Examples 7-8, Reynolds et al. teach a liquid dentifrice composition comprising calcium-bound  $\alpha$ -casein and “flavouring” which is considered to be a confection. This anticipates claim 43.

\* Examiner note: claim 45 is directed to a phosphoprotein preparation comprising the cross-linked the phosphoprotein. Thus, claims 45 and dependent claims therefrom are not included in the rejections by US Pat Nos. 5981475 and 5130123.

### ***Conclusion***

No claims are allowed.

### ***Discussion of the art***

The prior art made of record and not currently relied upon in any rejections is considered pertinent to Applicants' disclosure:

[1] Wilkinson P. C. (1972) teaches that casein preparation is usually insoluble in neutral solution (see page 1051, left column, 2<sup>nd</sup> paragraph).

[2] Wikipedia (2008, updated) Calcium phosphate, [http://en.wikipedia.org/wiki/Calcium\\_phosphate](http://en.wikipedia.org/wiki/Calcium_phosphate), page 1) teaches chemical structure of calcium phosphate “ $\text{Ca}_3(\text{PO}_4)_2$ ”.

[3] Sparre et al. (*Diabetologia* (2003) 46, 1497-1511) teach that  $\alpha_{s1}$ -casein which has molecular weight of 24529 daltons (se page 1504, Table 1).

[4] Winter et al. (US Pat. No. 4261819) disclose the crosslinked casein (see columns 1-2). However, this patent doe snot teach usefulness or a dentinal or a pharmaceutical composition comprising the said crosslinked casein. Thus, this patent is not considered to be prior art.

[5] Aboumahmoud et al. (*J. Dairy Sci.* (1990) 73, 256-263, from IDS filed 4/15/05) teach transglutaminase mediated cross-linked casein polypeptides. Yet, this article does not teach usefulness or dentinal/pharmaceutical composition comprising the said crosslinked casein. Thus, this article is not considered to be prior art.

[6] Vitkova et al. (*Czech J. Food Sci.* (2002) 20, 53-62) teach that UHT milk contains endogenous proteases which hydrolyze the milk protein including caseins (page 54, left column, 2<sup>nd</sup> paragraph, lines 1-6).

[7] Carbonaro et al. teach that milk contains, and milk casein binds calcium ions and calcium phosphate ions (see page 422, left column, last paragraph, lines 4-12, and Table 2).

[8] Stefanie (Argonne (2008, updated) Toothpaste –Suspension or solution, <http://www.newton.dep.anl.gov/askasci/chem03/chem03984.htm>, pages 1-3) teaches that toothpaste is considered to be a colloidal dispersion or an emulsion.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Wei Liu whose telephone number is 571-272-0949. The examiner can normally be reached from 9:00 a.m. to 5:00 p.m. on weekdays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Weber, Jon, can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703 308-4242 or 703 872-9306 (official) or 703 872-9307 (after final). Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 305-4700.

S. W. L./  
Examiner, Art Unit 1656  
March 11, 2008

/Karen Cochrane Carlson, Ph.D./

Primary Examiner, Art Unit 1656

